REMARKS

The Office Action dated July 3, 2003 presents the examination of claims 1-7. Claims 1-5 are withdrawn from consideration[1]. Claims 6 and 7 are amended. No new matter is inserted into the application.

Information Disclosure Statement

The Examiner requests copies of the following references: JP-A449246, (1992), Kawa et al., *Japanese Pharmacology & Therapeutics*, 24:149-152, (1996), and Matsumoto et al., *Jikken Igaku*, 15(9), (1997). In response to the Examiner's request, Applicants submit herewith under separate cover an Information Disclosure Statement (IDS) containing a PTO-1449 form listing EP 0 462 549 A1 (which is the European equivalent of JP-A449246), Kawa et al., and Matsumoto et al. An explanation of the relevance of each reference not in English is also provided in the IDS. The Examiner is respectfully requested to consider these references and initial and return the PTO-1449 form to Applicants as evidence of her consideration.

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[1] Applicants note that the status of claims 1-5 in the "Disposition of the Claims" section on page 1 of the Office Action has been incorrectly filled out. These claims are withdrawn from consideration rather than allowed.

Specification

The Examiner objects to the title of the present application and requires a new title indicative of the elected invention. In response to the Examiner's remarks, the former title is deleted and replaced with --METHOD FOR TREATMENT OF RENAL FAILURE AND OCCLUSIVE LESION OF BLOOD VESSELS BY ADMINISTRATION OF HEPATOCYTE GROWTH FACTOR--. Thus, the instant objection is overcome.

Claim Objections

The Examiner objects to claims 6 and 7 for minor typographical errors. Claims 6 and 7 are amended according to the Examiner's suggestion. Thus, the instant objection is overcome.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 6

The Examiner rejects claim 6 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by the specification. Applicants respectfully traverse. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that the specification enables a method for treating acute renal failure comprising administering an effective amount of HGF by continuous intravenous administration to a patient suffering from acute renal failure, but does not enable a method for treating or preventing renal disease comprising administering an effective amount of HGF by continuous intravenous administration.

Specifically, the Examiner asserts that the specification shows that HGF treats acute renal failure, but does not show that HGF has the ability to treat other types of renal diseases, such as systemic lupus erythematosus, diabetic nephropathy, kidney transplant, nephro-urinary tumor, and drug-induced renal disorder, etc. In particular, the Examiner notes that the disease model used in the specification is traditionally a model for acute renal failure, rather than any type of renal disease.

Claim 6 is amended to recite "renal failure" rather than "renal disease." Even though the Examples of the specification specifically show treatment of acute renal failure, the present invention encompasses a method for treating both acute and chronic renal failure. As described in the specification on page 2, lines 4-24, it is well known to a person skilled in the art that HGF is

useful for treating both acute and chronic renal failure. Furthermore, the specification describes that acute renal failure is caused by tubulorrhexis (see, page 2, line 8 of the specification). It is known in the art that chronic renal failure is caused by deterioration of renal tubes (see, EP 0 462 549 A1, included in the IDS of even date herewith). Accordingly, both acute and chronic renal failures have substantially the same pathologies. The present invention provides a method for administering HGF by continuous intravenous administration rather than the conventional bolus administration. The person skilled in the art can readily understand that the method of the present invention is effective in all types of renal failure, including acute and chronic renal failures.

The Examiner also asserts that it would cause the skilled artisan undue experimentation to determine an "effective amount" of HGF. Applicants respectfully disagree. The phrase "effective amount" is acceptable since the amount would be readily ascertainable to the skilled artisan. For example, the instant specification discloses specific doses for the treatment of renal disease and occlusive lesion of blood vessel on page 9, lines 4-11. Applicants note that the most recent case law has accepted the

phrase "an effective amount" even in the absence of a function to be achieved. In Ex parte Skuballa, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a claim which recited "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected. Since the instant specification clearly discloses guidelines for dosage and the intended utilities of HGF, the rejection over use of the phrase "an effective amount" is improper and must be withdrawn.

Further, the Examiner notes that the claim does not define a patient population. In response to the Examiner's remarks, claim 6 is amended to recite the patient population.

Finally, the Examiner asserts that the specification is not enabling for prevention of any renal disease. In order to overcome this aspect of the rejection, "preventing" is deleted from the claim.

Applicants respectfully submit that claim 6 is fully enabled by the specification. Withdrawal of the instant rejection is therefore respectfully requested.

Claim 7

The Examiner also rejects claim 7 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by the specification. Applicants respectfully traverse. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Again, the Examiner asserts that the phrase "occlusive lesion of blood vessel" is unduly broad, and that the specification enables only the treatment of "acute renal failure." The Examiner notes that the specification asserts that the glycerol model is a model of occlusive lesion of blood vessel. The Examiner disagrees and points to Kudo '388 (U.S. Patent 6,436,388), which allegedly discloses that the glycerol model is not utilized as a disease model for occlusive lesion of blood vessels.

Applicants respectfully disagree with the Examiner's assertions and provide further evidence (attached hereto as Exhibit 1) showing that continuous administration of HGF is effective for treating occlusive lesion of blood vessels. Specifically, the data shows that the continuous administration of HGF in a rabbit hindlimb ischemia model provided for an improved I/N ratio over continuous

administration of a control. The rabbit hindlimb ischemia model is a disease model for occlusive lesion of blood vessels.

The Examiner also asserts that it would cause the skilled artisan undue experimentation to determine an "effective amount" of HGF. Applicants respectfully disagree for the reasons presented above. Further, the Examiner notes that the claim does not define a patient population. In response to the Examiner's remarks, claim 7 is amended to recite the patient population.

Finally, the Examiner asserts that the specification is not enabling for prevention of occlusive lesion of blood vessel. In order to overcome this aspect of the rejection, "preventing" is deleted from the claim.

Applicants respectfully submit that claim 7 is fully enabled by the specification. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 6 and 7 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

First, the Examiner requests that the abbreviation of "HGF" be completely spelled out in the claims. Claims 6 and 7 are amended accordingly.

Second, the Examiner requests that the intended patient population be recited in the claims. Claims 6 and 7 are amended accordingly.

Finally, the Examiner asserts that the phrase "occlusive lesion of blood vessel" recited in claim 7 is unduly broad. Applicants respectfully disagree for the reasons described above. Specifically, the further data presented as Exhibit 1 shows that the method of the present invention is effective for treating occlusive lesion of blood vessels.

Applicants respectfully submit that the instant claims particularly point out and distinctly claim the subject matter of the instant invention such that the claims fully comply with 35 U.S.C. § 112, second paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 6 and 7 under 35 U.S.C. § 102(b) for allegedly being anticipated by Kawa et al. (*Jpn Pharmacol*

Therapy, 24(Suppl 1):149-152, 1996). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

In order to overcome this rejection, claims 6 and 7 are amended to recite the specific patient population that is administered HGF. Kawa et al. fails to disclose a continuous intravenous administration of HGF to a patient suffering from renal failure or to a patient suffering from occlusive lesion of blood vessel.

For these reasons, Kawa et al. fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome all rejections/objections of record. The present application is now in condition for allowance. The Examiner is respectfully requested to issue a Notice of Allowance indicating that claims 6 and 7 are allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully

requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
John W. Bailey, #32,881

JWB/KLR:gmh

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

Attachment(s): Exhibit 1

Comparative Example

Study on continuous administration of HGF in rabbit hindlimb ischemia model

NZW rabbits (male, 3-4 kg weight) were used and were anesthetized. Rabbit hindlimb ischemia model was produced by dissecting a left femoral region and removing a left femoral artery. From 10 days after the removal of the femoral artery, a continuous infusion of HGF (1 mg) or a vehicle was performed for one hour through an auricle vein (once a day, for 5 days). At 40 days after the removal of the femoral artery, the rabbits were anesthetized, and blood pressures of hindlimbs were measured. The I/N ratio (%) = blood pressure in an ischemic limb/blood pressure in a normal limb x 100 was calculated from blood pressures in the normal limb and ischemic limb, and evaluated. The results (I/N ratio) are shown in the following figure.

As shown in the figure, the I/N ratio was improved in the HGF administration group in comparison with the vehicle administration group.